

is heterologous to the wild-type gene product. In view of the foregoing, the rejections under 35 U.S.C. § 112, first paragraph, are obviated and should be withdrawn.

**2. THE REJECTIONS UNDER 35 U.S.C. § 103
SHOULD BE WITHDRAWN**

Claims 1, 4, 7-12, 16, 17, 20, 21, 25-32, 39, and 46-48 are rejected under 35 U.S.C. § 103 (a) as obvious over Walsh et al., 1991, J. Clin. Res. 39(2):325A ("Walsh I") in view of U.S. Patent No. 5,436,146 (the "'146 patent"), optionally further in view of Ohi et al., 1990, Gene 89:279-282 ("Ohi"). Claim 33 is rejected under 35 U.S.C. § 103 (a) as obvious over Walsh I in view of the '146 patent. The Examiner contends that it would have been obvious to one of ordinary skill in the art to combine the tissue-specific regulatory elements taught by the '146 patent with the wild-type globin gene taught by Walsh I to obtain the claimed recombinant adeno-associated virus ("AAV") vector. The Examiner further contends that it would have been obvious to one of ordinary skill in the art in view of the '146 patent and Ohi to omit a selectable marker from an AAV vector to allow for the insertion of a larger foreign sequence. For the reasons detailed below, Applicants respectfully request that this rejection be withdrawn.

A finding of obviousness requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Graham v. Deere 383 U.S. 1 (1996). The proper inquiry is whether the art suggests the invention, and whether the art provides one of ordinary skill in the art with a reasonable expectation of success. In re O'Farrell 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicants' disclosure. In re Vaeck 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants have canceled Claims 4, 7, 9-12, 16, 17, 21, 25-32, 47, and 48 and amended Claims 1, 8, 16, 19, 20, 33, and 39 to more particularly point out and distinctly claim the invention. The claims, as amended, recite a recombinant AAV vector comprising a eukaryotic based nucleic acid sequence encoding a wild-type gene product controlled by a

eukaryotic based *cis*-acting regulatory sequence chosen from the region located from about hypersensitive site I to about hypersensitive site VI of the human globin gene cluster, which is heterologous to the wild-type gene product. The cited art does not contemplate, suggest or teach the recombinant AAV vectors of the present invention. Walsh I merely teaches a recombinant AAV vector consisting of a globin gene under the control of a portion of the regulatory element native to the globin gene which expresses the globin gene *in vitro* upon transduction into a cultured cell line. Shenk teaches recombinant adeno-associated virus vectors for use in the production of helper-free AAV stocks. Ohi merely teaches the construction and replication of an AAV expression vector containing human β -globin cDNA under the control of the AAV p40 promoter. Neither Walsh I, Shenk, nor Ohi teach or suggest an AAV vector comprising a eukaryotic nucleic acid sequence encoding a wild-type gene product whose expression is controlled by a eukaryotic *cis*-acting regulatory sequence chosen from the region located from about hypersensitive site I to about hypersensitive site VI of the human globin gene cluster which is heterologous to the wild-type gene product. Further, neither Walsh I, Shenk, nor Ohi teach or suggest an AAV vector comprising a eukaryotic nucleic acid sequence encoding a wild-type gene product which is expressed in a mammalian host in an immune cell specific manner upon introduction of an immune cell stably transduced with the AAV vector. Thus, the cited references, alone or in combination, do not teach nor suggest the recombinant AAV vectors of the claimed invention. Therefore, the cited references cannot be combined to establish a *bona fide prima facie* case of obviousness under 35 U.S.C. § 103, and the rejection should be withdrawn.

CONCLUSION

Applicants respectfully request consideration and entry of the foregoing amendments and remarks. It is believed that the application is now in condition for allowance. An early and favorable action on the merits is earnestly solicited.

Date: May 22, 2000

Respectfully submitted, by *Jacqueline Penn*
Reg No. 43,492
Laura A. Coruzzi 30,742

Laura A. Coruzzi (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosure

G